REMARKS

Claims 31-37 and 40 have been canceled, without prejudice or disclaimer. Applicants reserve the right to pursue these claims in continuing patent application(s). Claims 41-45, 48-52, and 55 are pending. Claims 41, 44, 48, 49, 52, and 55 are amended. A non-final Office Action in the present case was mailed on May 26, 1999, and the present case was suspended pursuant to a USPTO Communication dated May 1, 2000.

Pursuant to the Examiner's request, claims 41 and 49 have been amended to recite "comprising." This term indicates that any other elements can be included in the claimed invention. While applicants believe that the original claim term "containing" carries the same meaning as "comprising," this amendment is made to advance prosecution, and does not constitute surrender of any subject matter encompassed by the claims.

Pursuant to the Examiner's request, the stringent hybridization conditions recited in the specification, at pages 14-15, are now recited in claims 48 and 55. Applicants note that an obvious clerical error in the specification at page 15, lines 13-14, has been corrected by the present amendment to the specification. The specification states at lines 13-14, page 15, "5 x SSC (0.75 M NaCl, 0.075 M Sodium pyrophosphate." However, one of skill in the art would immediately recognize the clerical error, because 5 x SSC is composed of 0.75 M NaCl and 0.075 M Sodium citrate, not pyrophosphate. Another type of solution used in hybridization is "SSPE", which does employ sodium pyrophosphate, but that solution also employs EDTA, which is not mentioned in this passage. Accordingly, one of skill in the art would recognize that the "pyrophosphate" is a clerical error and should say "citrate." Accordingly, the amendment to the specification which changes "pyrophosphate" to "citrate" does not add new matter.

Pursuant to the Examiner's request, claims 44 and 52 now recite that the fusion protein comprises a heterologous amino acid sequence. Support for this amendment can be found on page 16. While applicants believe that the original claim term "not naturally associated with" carries the same meaning as "heterologous," this amendment

is made to advance prosecution, and does not constitute surrender of any subject matter encompassed by the claims.

The Examiner requested clarification of what is meant by the domains recited in claims. The domains recited in these claims are described in the specification.

With respect to Claims 42 and 43, Figure 2A indicates that a PH domain is amino acids 25-169. See also figure description for Figure 2A on 8. Also, page 11, line 31, through page 12, line 5, describes that the PH domain is "pleckstrin homology" domain. As indicated in Figure 2A, amino acids 192-234 denote the SH3 domain, and amino acids 296-375 denote the SH2 domain. As noted in references Hamaguchi and Tamagnone, submitted herewith, these "SH" domains are "src homology" domains, which also are discussed on pages 11-12. Finally, Figure 2A illustrates that amino acids 424-659 denote the TK domain, which is the "tyrosine kinase" domain, which is also known as the catalytic domain. See also Figure 2A legend on page 8, which indicates that Figure 2A shows the "PH," "SH2," "SH3" and "catalytic" domains. The Examiner will note that tyrosine kinases typically are termed "TK." See specification, page one, line 33.

In the same vein, the domains recited in claims 50 and 51 are described in the specification. Figure 3A shows the positions of the SH2 (amino acids 122-201), SH3 (amino acids 54-112), and TK (amino acids 247-486) domains. See also legend for Figure 3A on page 8.

Applicants have also submitted references for consideration by the Examiner. Reference Cance (1994) was cited and considered by the Examiner in related application (Ser. No. 08/232,545), see PTO-892 dated 9/27/95. Pursuant to 37 CFR 1.98(d), this reference is listed on the enclosed 1449 form, but a copy has not been provided. Applicants also submit references which were cited during prosecution of U.S. Ser. No. 08/320,432 (Alitalo, K.), and applicants also submit references Tamagnone (1994) and Hamaguchi (1994).

Conclusion

It is respectfully urged that the present claims are in condition for allowance and an early notice to this effect is earnestly solicited.

Should there be any questions, the Examiner is invited to contact the undersigned at the telephone number shown below.

Respectfully submitted,

Date May 31, 2001

By _____

FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5109
Telephone: (202) 672-5414
Facsimile: (202) 672-5399

Beth A. Burrous
Attorney for Applicant
Registration No. 35,087

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Marked up rewritten specification paragraph from page 1:

This application is a continuation-**in-part** application of United States Application Serial Number 08/232,545, filed April 22, 1994, which is incorporated herein by reference.

Marked up rewritten specification paragraph from pages 14-15:

Due to the inherent degeneracy of the genetic code, other DNA sequences which encode substantially the same or a functionally equivalent amino acid sequence, may be used in the practice of the invention for the cloning and expression of the MKK protein. Such DNA sequences include those which are capable of hybridizing to the human MKK sequence under stringent conditions. The phrase "stringent conditions" as used herein refers to those hybridizing conditions that (1) employ low ionic strength and high temperature for washing, for example, 0.015 M NaCl/0.0015 M sodium citrate/0.1% SDS at 50°C.; (2) employ during hybridization a denaturing agent such as formamide, for example, 50% (vol/vol) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50 mM sodium citrate at 42°C; or (3) employ 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M Sodium **citrate)** **[pyrophosphate]**, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 g/ml), 0.1% SDS, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC and 0.1% SDS.

Marked up rewritten claims:

48. (Amended) An isolated protein which is encoded by a naturally occurring nucleic acid molecule which hybridizes under highly stringent conditions to the nucleic acid sequence which encodes the polypeptide of SEQ ID NO:4**, wherein said stringent conditions are selected from the group consisting of:**

(a) 0.15 M NaCl/0.0015 M sodiumcitrate/0.1% SDS at 50°C for washing;

(b) 50% (vol/vol) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50mM sodium phosphate buffer at pH 6.5 with 750 mM NaCl and 75 mM sodium citrate at 42°C during hybridization; or

(c) hybridzation in 50% formamide, 5 x SSC, 5 x Denhardt's solution, 50 g/ml sonicated salmon sperm DNA, 0.1% SDS, and 10% dextran sulfate at 42°, with washes at 42° in 0.2 x SSC and 0.1% SDS.

41. (Amended) An isolated protein **comprising** **[containing]** the amino acid sequence shown in SEQ ID NO:4.

44. (Twice Amended) A fusion protein comprising the isolated protein of Claim 41 or 42 fused to **a heterologous** **[an]** amino acid sequence **[not naturally associated with the isolated protein of Claim 41 or 42]**.

49. (Amended) An isolated protein **comprising** **[containing]** the amino acid sequence shown in SEQ ID NO:6.

52. (Twice Amended) A fusion protein comprising the isolated protein of Claim 49 or 50 fused to **a heterologous** **[an]** amino acid sequence **[not naturally associated with the isolated protein of Claim 41 or 42]**.

55. (Amended) An isolated protein which is encoded by a naturally occurring nucleic acid molecule which hybridizes under highly stringent conditions to the nucleic acid sequence which encodes the polypeptide of SEQ ID NO:6**, wherein said stringent conditions are selected from the group consisting of:**

(a) 0.15 M NaCl/0.0015 M sodiumcitrate/0.1% SDS at 50°C for washing;

(b) 50% (vol/vol) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50mM sodium phosphate buffer at pH 6.5 with 750 mM NaCl and 75 mM sodium citrate at 42°C during hybridization; or

(c) hybridzation in 50% formamide, 5 x SSC, 5 x Denhardt's solution, 50 g/ml sonicated salmon sperm DNA, 0.1% SDS, and 10% dextran sulfate at 42°, with washes at 42° in 0.2 x SSC and 0.1% SDS.